

# *Ab Initio* Calculations and Molecular Mechanics (MM3) Force Field Development for Ammonium and Protonated Aliphatic Amines

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**ABSTRACT:** The geometries and vibrational frequencies of 11 training molecules containing the ammonium ion moiety were calculated at the MP2/6-31 + G\* level of theory. Various torsional energy profiles were also calculated using this basis set. From those *ab initio* calculations, a molecular mechanics (MM3) force field was developed using our Parameter Analysis and Refinement Toolkit System (PARTS). Using this set of parameters, the MM3 force field was found to well reproduce the molecular geometries and vibrational spectra for the all training molecules. CPU time was reduced from days to seconds. The availability of this new force field dramatically increases the feasibility of the computer-assisted drug design involving ammonium and protonated amino groups. © 1997 by John Wiley & Sons, Inc. *J Comput Chem* **18**: 1371–1391, 1997

**Keywords:** molecular mechanics; MM3; PARTS; force field; protonated amine; *ab initio*

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## Introduction

The excitatory neurotransmitter glutamate has an extensive role in the central nervous system (CNS). Our studies have focused on the N-

methyl-D-aspartate (NMDA) receptor subtype, with emphasis on investigation of analogs of 1-aminocyclopropanecarboxylic acid (ACPC) and of kynurenic acid (KYNA) in connection with the strychnine-insensitive glycine site. Based on comparison of equipotential surfaces and conformational analysis we had concluded that a zwitterionic  $\alpha$ -amino acid is required for high affinity binding<sup>1</sup> at the strychnine-insensitive glycine site. However, our studies were limited by the lack of validated parameters for the modeling of zwitterionic species.

Molecular modeling has become an increasingly important tool in medicinal chemistry, serving to gain insights into biochemical mechanisms and to assist in the design of molecules with specific biological activities. For example, SAR, CoMFA, and conventional QSAR models have been demonstrated to provide useful predictive information in the series of 3 $\beta$ -phenyltropan-2 $\beta$ -carboxylate analogs of cocaine.<sup>2</sup> In some of our previous studies the AM1 Hamiltonian method<sup>3</sup> was utilized for the final geometry optimization and charge calculation with various solvation models. However, although mutations of the dopamine transporter (DAT) have demonstrated that aspartic acid at position 79 is involved in the transport of dopamine and of the neurotoxin 1-methyl-4-phenylpyridinium (MPP<sup>+</sup>) and in the binding of the cocaine analog (-)-2- $\beta$ -carbomethoxy-3 $\beta$ -(4'-fluorophenyl)tropane (WIN 35,428),<sup>4</sup> suggesting that a charged nitrogen atom is involved, the fact that none of this solvation model was developed based on a similar ionic system limited our effort to apply a quantum mechanical approach to this problem. In MM3, however, a solvation effect can be approximated by using an appropriate dielectric constant. Whereas the unprotonated amine may provide a useful approximation of the protonated amine in the relatively rigid and conformationally homogeneous cocaine skeleton, this approximation is likely not to apply in other cases.

Nitrogen-containing molecules are involved in a very large number of physiological events. In many of these compounds the nitrogen atom is basic; that is, it is part of an amino group and, thus, may be protonated at physiological pH. The physiologically active form of the amine, however, may, or may not, be the protonated form. To develop meaningful models of physiologically active agents it is, therefore, imperative to model ammonium ions. The optimization of protonated amines can, of course, be carried out using *ab initio* methods. However, these computations require vast

amounts of computer time, disk space, and memory to treat most molecules of interest. For example, the CPU time requirements for *ab initio* calculations at the Hartree-Fock level of theory are proportional to  $n^4$ , where  $n$  is the number of atomic orbitals in the molecule. For the calculations with Møller-Plesset correlation or configuration interaction the proportionality factor may go even higher. Manageable computational time can be achieved by using molecular mechanics (MM) where the computational time is proportional to  $m^2$ , where  $m$  represents the number of atoms, not orbitals. Furthermore, for well-parameterized force fields, such as those in MM3,<sup>5</sup> the accuracy of MM calculations usually exceeds that of quantum chemical methods. Based on these considerations, the determination of the specialized set of parameters required for protonated amino groups was undertaken. In the present study, the atomic interactions for relatively small groups (training molecules) with similar chemical environment were studied using the *ab initio* method. Based on the properties (geometry and vibrational frequencies) of those training molecules, a set of MM3 force field parameters was developed. The parameters developed were applied to ethylene diamine, a model for polyamines, which, in addition to other physiological functions, are modulators of the NMDA receptor<sup>6</sup> as well.

## Computational Method

A molecular system in MM3,<sup>5,7,8</sup> as well as in other molecular mechanics schemes, is a collection of atoms interacting with one another. The interactions can be described in classical mechanics in terms of energy equations. The total potential energy in MM3 may be expressed as:

$$E_{\text{MM3}} = \sum (E_{\text{str}} + E_{\text{bend}} + E_{\text{tors}} + E_{\text{VDW}} + E_{\text{dipole}} + E_{\text{bend-bend}} + E_{\text{str-bend}} + E_{\text{tors-str}})$$

where the energy terms included are stretching, bending, torsion, van der Waals, dipole-dipole (including charge-dipole and charge-charge for the system with net charges), stretch-bend, and torsion-stretch.

Each energy term depends on several adjustable parameters. For example, the stretching terms are controlled by the equilibrium bond lengths and the stretching force constants, which are unique for every combination of atoms A-B. The torsional energy term consists of three torsional parameters,

$V_1$ ,  $V_2$ , and  $V_3$ . A force field with "appropriate parameters" is able to predict various molecular properties ranging from geometry (bond lengths, bond angles, torsion angles), physical properties (moments of inertia, dipole moments), to vibrational frequencies and thermochemical values. On the other hand, the development of force field parameters depends on the availability of reliable values for these measurable physical properties. In the absence of reliable experimental data, *ab initio* calculations are another source that may be used to develop and check the behavior of a force field. This approach has been applied successfully in our laboratories for many different functional groups over the years.

For our investigations of zwitterionic  $\alpha$ -amino acids and of polyamines as modulators of the NMDA subtype of the glutamatergic system, a force field that can be used to simulate the behavior of protonated amine(s) is required. Nonproto-

nated nitrogen has been parameterized (atom type 8) in previous studies<sup>9,10</sup> of aliphatic amines. The parameters that remain unknown (or need to be further improved) are those associated with the protonated nitrogen,<sup>11</sup> namely ammonium ions. As shown in Figure 1, 11 training molecules were used for the general parameterization of ammonium ions, including ammonium, 1, methylammonium, 2, dimethylammonium, 3, trimethylammonium, 4, tetramethylammonium, 5, ethylammonium, 6, *trans*-propylammonium, 7, *gauche*-propylammonium, 8, *trans*-ethylmethylammonium, 9, *gauche*-ethylmethylammonium, 10, *trans*-ethyldimethylammonium, 11. A full geometry optimization was carried out for each of the structures (1–11) before calculating the second derivative and vibrational frequencies. All *ab initio* calculations were on the MP2/6-31 + G\* level of theory using Gaussian94<sup>12</sup> on an SGI/Indigo 2. Based on those *ab initio* calculated results, the

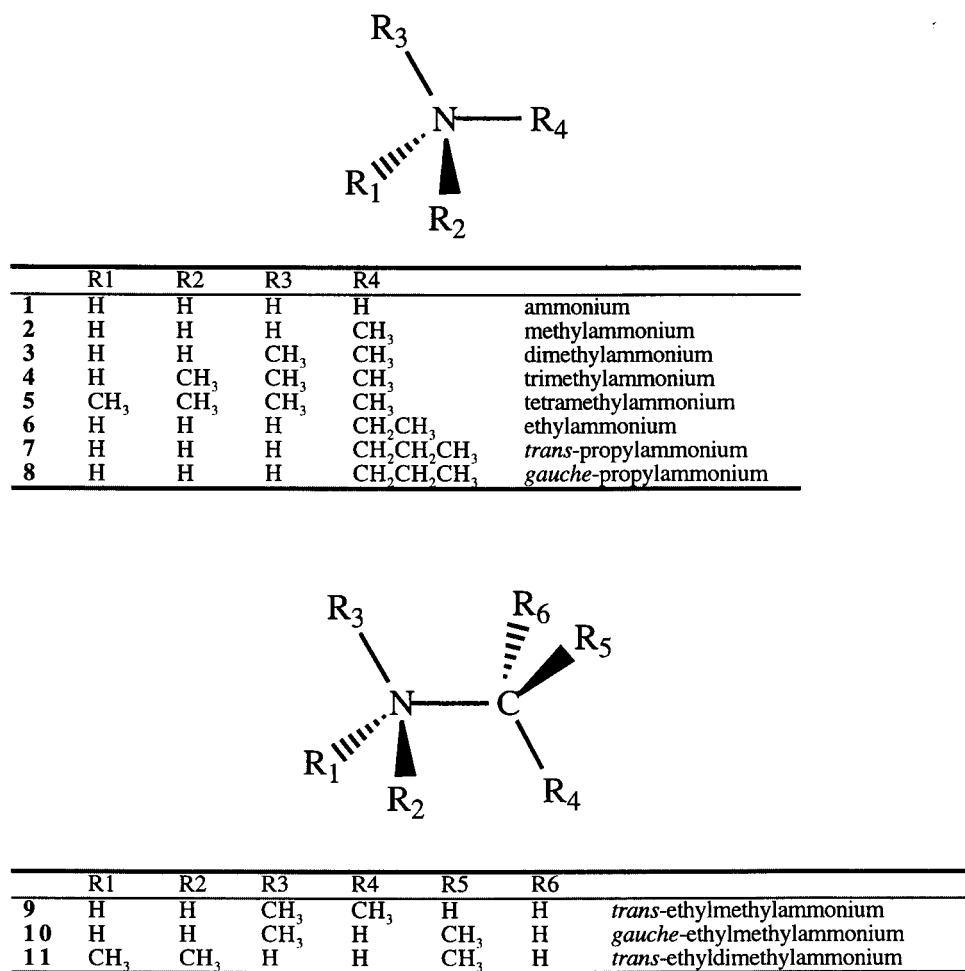


FIGURE 1. Training set of molecular structures used in the present study.

Parameter Analysis and Refinement Toolkit System (PARTS)<sup>13,14</sup> was used to develop the MM3 parameters that can best reproduce the calculated properties of those training molecules. During the process of the parameterization, PARTS monitors all the properties of interest (in the present study, it monitored bond lengths, bond angles, torsion angles, torsional energy profiles, dipole moments, vibrational frequencies, as well as eigenvectors associated with all vibrational modes) while iteratively adjusting the values of the force field parameters. Using the final optimized parameters, MM3 calculations were carried out. The comparisons between the MM3 and *ab initio* results are reported and discussed in the next section.

## Results and Discussion

### TORSIONAL ENERGY PROFILES AND BARRIERS

A torsional energy profile refers to a graph of potential energy versus the changes of the torsion angle of interest. In the cases of rotations with high symmetry, the torsional energy profiles also have symmetric patterns. For example, the rotations of a methyl group or an ammonium group generate torsional energy profiles with threefold symmetry, which eliminates the contributions of  $V_1$  and  $V_2$  terms. The rotations without any symmetry, on the other hand, have more complicated torsional energy profiles that require the mixing of all three torsional parameters ( $V_1$ ,  $V_2$ , and  $V_3$ ) defined in MM3-truncated Fourier series. The torsion potential energy surfaces were determined by the energy changes upon the changes of torsional angles. When a specific torsion angle changes, many MM3 energy components may also change (i.e., torsional energy, van der Waals, dipole-dipole, charge-dipole when it applied, various torsion-related cross-terms, as well as other minor changes such as stretching, bending energy components). All of these terms contribute to the overall shape of the surface. The breakdown components, while offering more detailed information about the intramolecular interactions, will take too much space to cover in this article; however, this information is available from authors upon request.

Six sets of torsional parameters were investigated for alkylammonium ions (Table I, Figs. 2–7). Because four of them ( $\text{H}-\text{N}^+-\text{C}-\text{H}$ ,  $\text{H}-\text{N}^+-\text{C}-\text{H}$ ,  $\text{H}-\text{N}^+-\text{C}-\text{C}$ ,  $\text{C}-\text{N}^+-\text{C}-\text{H}$ ) have threefold symmetry, only a  $V_3$  term is present in the torsional energy equation. As shown in Figure

2, because both the methyl and the ammonium group have threefold symmetric rotation, the torsional energy profile of methylammonium has three identical minima and transition states (in the range of  $360^\circ$ ). MM3 and Gaussian are in a close agreement for this energy profile with the height of the barriers being 2.55 kcal/mol from both methods. After the torsional parameter of  $\text{H}-\text{N}^+-\text{C}-\text{H}$  has been determined from the curve of methylammonium, the value of the torsional parameter for  $\text{H}-\text{N}^+-\text{C}-\text{C}$  is only dependent on the torsional energy profile of ethylammonium. Using the final parameter set, the energy curve of MM3 is almost identical to the one from the *ab initio* calculations with barriers of 2.70 kcal/mol between three identical minima (Fig. 3). Another torsion angle present in ethylammonium is  $\text{N}^+-\text{C}-\text{C}-\text{H}$ . The torsional energy profile of this angle also has a threefold symmetry originated from the terminal methyl group. This methyl rotation carries a higher energy barrier than methylammonium, which may be attributed to the dipole-induced dipole interaction between the  $\text{C}-\text{N}^+$  and  $\text{C}-\text{H}$  bonds. As indicated in Fig. 4, MM3 has a barrier of 3.35 kcal/mol, whereas the one from the *ab initio* calculation is 3.44 kcal/mol. The torsional energy profile of propylammonium is controlled by four torsional parameters:  $\text{N}^+-\text{C}-\text{C}-\text{C}$ ,  $\text{N}^+-\text{C}-\text{C}-\text{H}$ ,  $\text{H}-\text{C}-\text{C}-\text{C}$ , and  $\text{H}-\text{C}-\text{C}-\text{H}$ . Among them,  $\text{N}^+-\text{C}-\text{C}-\text{C}$  is the only undetermined one. By changing the values of this set (all  $V_1$ ,  $V_2$ , and  $V_3$ ), the MM3 potential energy surface can be altered. With the final parameter set, MM3 closely reproduced the *ab initio* calculated curve (Fig. 5). According to both the MP2/6-31 +  $G^*$  and MM3 calculations, three possible minima exist, corresponding to two *gauche* conformations and one *trans* conformation. The energy difference between the *gauche* and *trans* conformation, however, is negligible. The energy barrier between the *gauche* and *trans* conformers is 3.8 kcal/mol, whereas the one between the two *gauche* conformers is 5.3 kcal/mol. Similarly, torsional parameters of  $\text{C}-\text{N}^+-\text{C}-\text{H}$  and  $\text{C}-\text{N}^+-\text{C}-\text{C}$  were developed based on dimethylammonium and ethylmethylammonium. Their torsional energy profiles are shown in the supplementary material.

Two additional sets of torsional parameters,  $\text{N}^+-\text{C}-\text{C}-\text{N}^+$  and  $\text{N}^+-\text{C}-\text{C}-\text{N}$  (Figs. 6 and 7), exist for calculations involving protonated ethylenediamine. The steric interactions for these two cases are similar, and can be characterized by three local minima (two *gauche* conformers and one *trans* conformer) and three transition states. However,

**TABLE I.**  
**MM3 Parameters for Alkylammonium.<sup>a</sup>**

Atom 1	Atom 2	Atom 3	Atom 4	V <sub>1</sub>	V <sub>2</sub>	V <sub>3</sub>
Torsional parameters						
5 <sup>b</sup>	1	39	1	0.0000	0.0000	0.2617
1	1	39	1	−0.9836	−0.2402	0.3806
5	1	39	48	0.0000	0.0000	0.2121
1	1	39	48	−1.7326	0.3690	0.1592
5	1	1	39	0.0000	0.0000	0.428
1	1	1	39	−1.1684	0.0827	0.9924
39	1	1	39	−10.3820	−3.0210	0.6370
8	1	1	39	7.5820	−4.5880	1.6000
Atom 1		Atom 2		k <sub>s</sub>		l <sub>0</sub> (Å)
Stretching parameter						
48		39		6.1402		1.0283
1		39		4.2741		1.5031
Atom 1	Atom 2	End of bond		Attached atom		Correction to l <sub>0</sub>
Electronegativity correction parameters						
1	1	1		39	−0.0110	
5	1	1		39	−0.0128	
1	39	39		1	−0.0096	
48	39	39		1	−0.0061	
Atom 1		Atom 2		Bond moment		
Bond moments						
39		48		−1.9219		
1		39		−0.5265		
Atom 1	Atom 2	Atom 3	k <sub>q</sub>		θ <sub>0</sub> (°)	Type
Bending parameters						
48	39	48	0.6086		106.37	1 <sup>c</sup>
48	39	48	0.6086		106.97	2
48	39	48	0.6086		108.56	3
1	39	48	0.5210		105.95	1
1	39	48	0.5210		107.42	2
1	39	48	0.5210		108.52	3
1	39	1	0.7190		107.11	1
1	39	1	0.7190		110.00	2
1	39	1	0.7190		112.00	3
1	1	39	0.5430		109.30	2
1	1	39	0.5430		100.00	3
5	1	39	0.9000		104.70	2
5	1	39	0.9000		104.70	3

<sup>a</sup> These parameters were developed for MM3 and are not intended for MM2 or MM4.<sup>b</sup> The atom types for the atoms included are N<sup>+</sup> (39), N<sup>+</sup>—H(48), C(1), and H(5). The positive charge is localized at the central nitrogen.<sup>c</sup> For a bending term A—B—C, the angle type is 1 if B has no attached hydrogen (not counting A and C), the angle type is 2 if B has 1 attached hydrogen (not counting A and C), and the angle type is 3 if B has two attached hydrogens (not counting A and C).

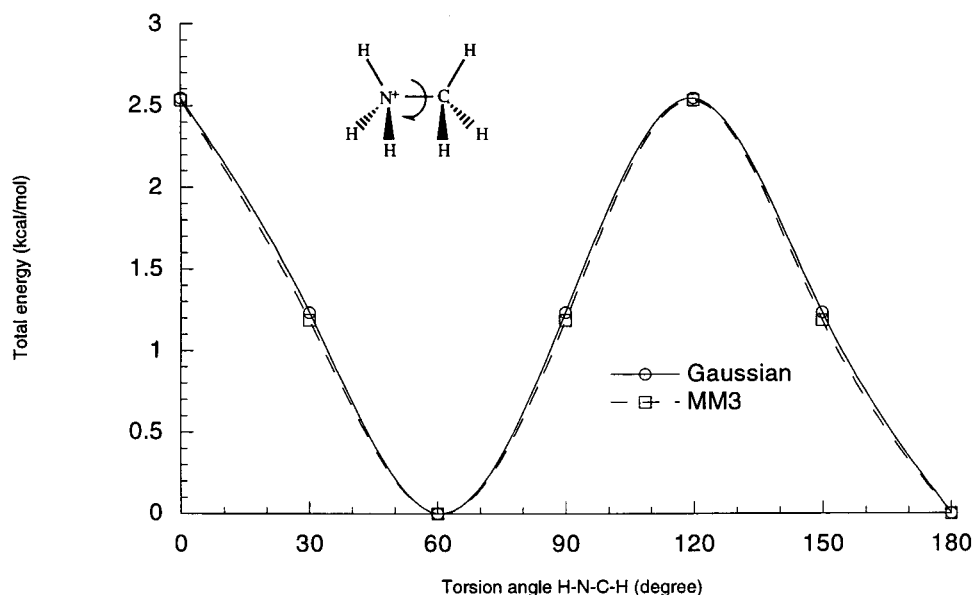


FIGURE 2. Torsional energy profile for  $\text{H}-\text{N}^+-\text{C}-\text{H}$ .

the dipole-dipole interaction for  $\text{N}^+-\text{C}-\text{C}-\text{N}^+$  strongly prefers the *trans* conformation, whereas the *gauche* conformers are virtually eliminated. On the other hand, the dipole-induced dipole interaction in  $\text{N}^+-\text{C}-\text{C}-\text{N}$  favors a closer distance between the two nitrogen atoms so that the *gauche* conformations are preferred even if the *trans* conformation still exists (with a potential energy 10 kcal/mol higher than the *gauche* conformer).

### AMMONIUM (1)

With a tetrahedral symmetry, ammonium has four identical bond lengths and six identical bond angles. Due to symmetry, the equilibrium  $\text{H}-\text{N}-\text{H}$  bond angle parameter does not affect the values of the bond angles in the final structure. This parameter, however, does affect the result of the calculation, especially the vibrational frequen-

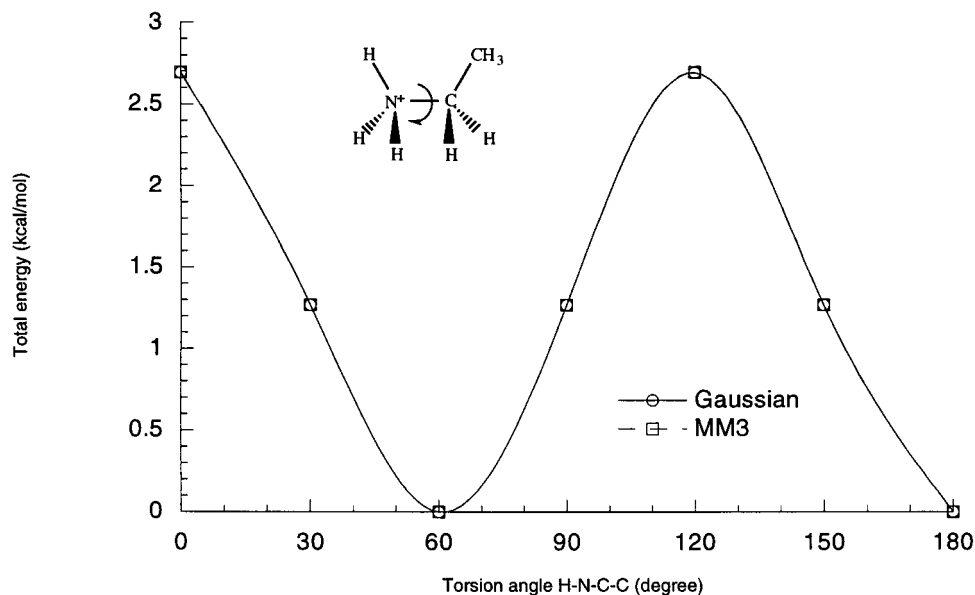


FIGURE 3.

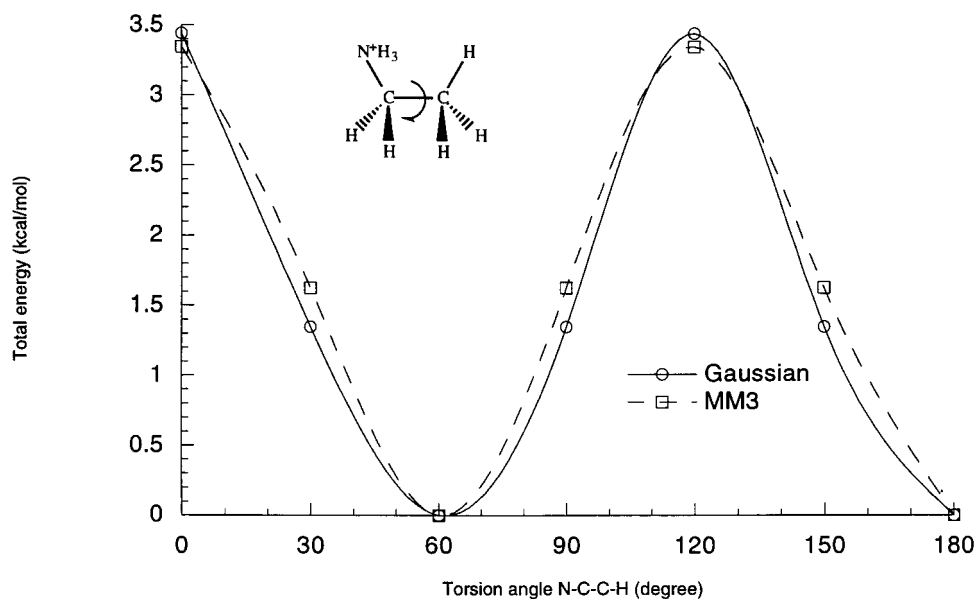


FIGURE 4.

cies, by placing the bond angles of H—N—H on different positions of the potential energy surface. For example, if the equilibrium bond angle has the same value as the final geometry, 109.5°, the bond angle H—N—H is at the bottom of the energy well, which has a different second derivative from the points on the slope. Consequently, this will cause a different result for the vibrational frequen-

cies. As can be observed in Table II, for the geometry, MM3 completely reproduces the geometry predicted by *ab initio* calculations, although the bond angle is actually controlled by symmetry rather than by the force field parameter. The spectrum of ammonium consists of four N—H stretching modes and five H—N—H bending modes. *Ab initio* calculated vibrational frequencies were used

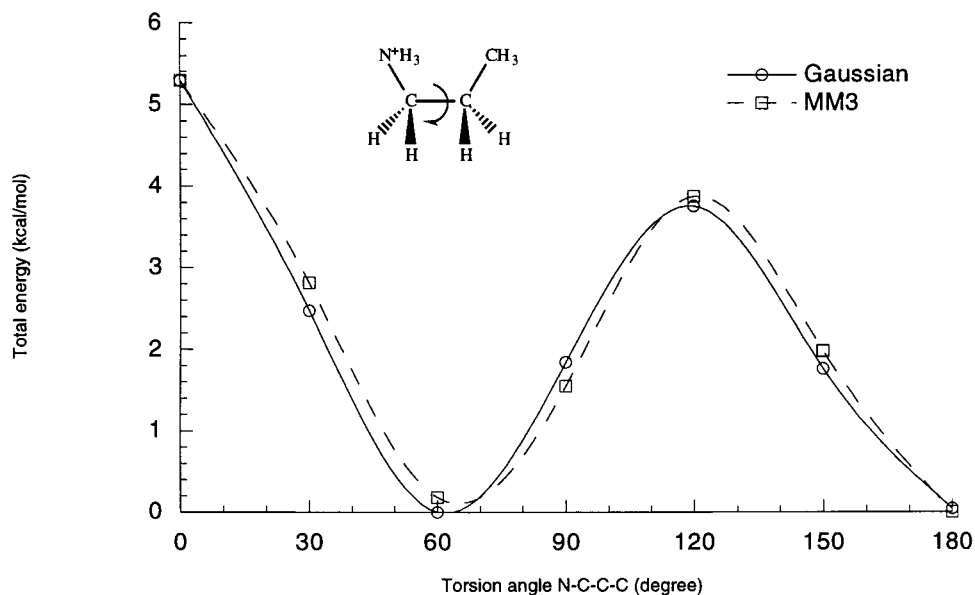


FIGURE 5.

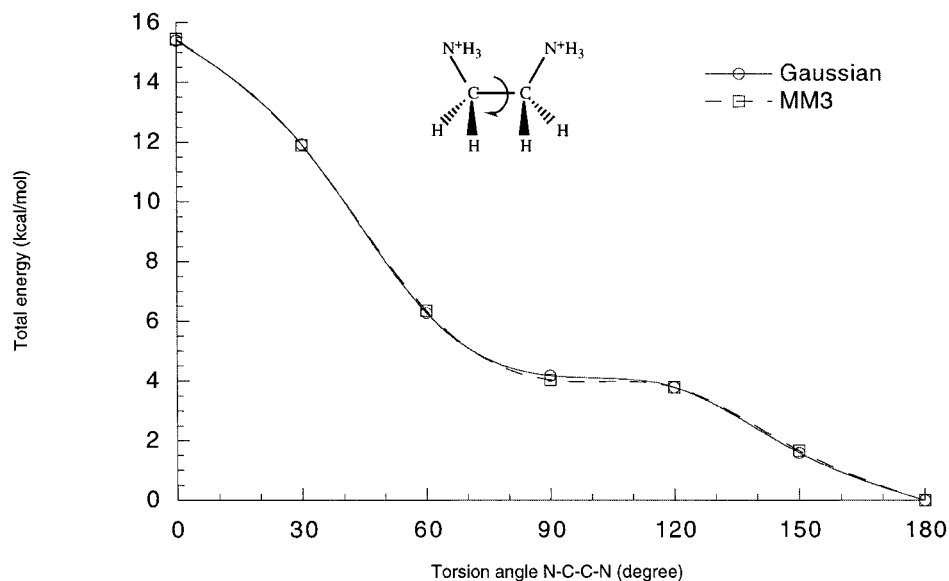


FIGURE 6. Torsional energy profile for  $\text{N}^+-\text{C}-\text{C}-\text{N}^+$ .

to calibrate the parameters of the force field. According to our previous experience,<sup>13,15</sup> a factor of 0.95 was used to scale the Gaussian vibrational frequencies calculated at the MP2/6-31 + G\* level of theory. As shown in Table I, while the asymmetric stretching modes carry a smaller discrepancy than the symmetric mode, the MM3 parameters provide overall good performance with a root-mean-square deviation of  $7\text{ cm}^{-1}$ .

#### METHYLAMMONIUM AND OTHER METHYL DERIVATIVES (2, 3, 4, AND 5)

All four ammonium methyl derivatives, methylammonium (2), dimethylammonium (3), trimethylammonium (4), and tetramethylammonium (5), were included in the molecular training set (Tables III–VI). In the case of methylammonium (2), the N—C bond is the only one between heavy

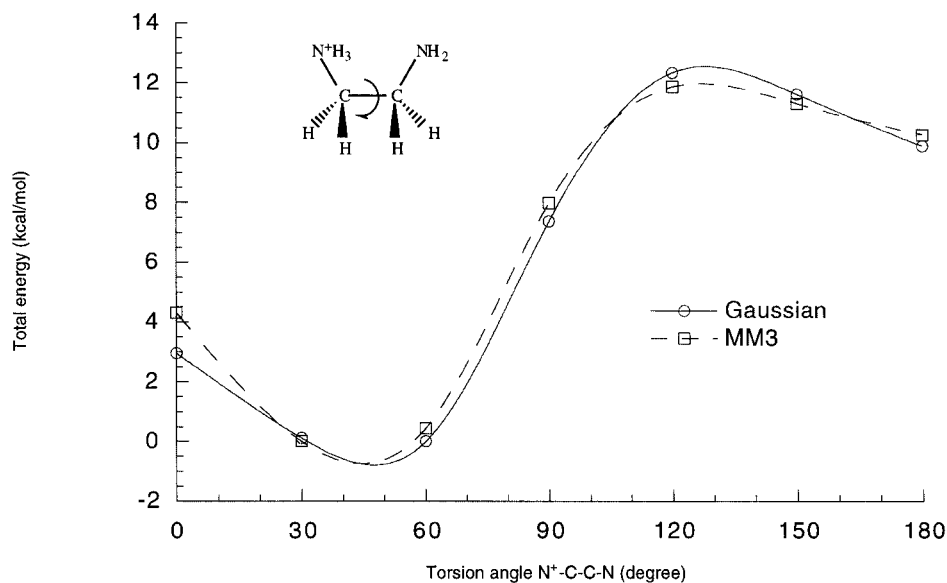


FIGURE 7. Torsional energy profile for  $\text{N}^+-\text{C}-\text{C}-\text{N}$ .



**TABLE II.**  
**Geometrical Data and Vibrational Frequencies**  
**of Ammonium.**

	Gaussian	MM3	Deviation
Bonds			
N(+)-H (average)	1.028	1.028	0.000
Angles			
H-N(+)-H (average)	109.5	109.5	0.0
Modes			
Asymm. N-H str.	3365	3370	5
Asymm. N-H str.	3365	3370	5
Asymm. N-H str.	3365	3370	5
Symm. N-H str.	3226	3214	-13
H-N-H bend	1685	1676	-9
H-N-H bend	1685	1676	-9
H-N-H bend	1460	1464	4
H-N-H bend	1460	1464	4
H-N-H bend	1460	1464	4
		rms	7

atoms, in which MM3 and Gaussian are in a close agreement with bond lengths of 1.510 Å and 1.515 Å, respectively. Upon increasing the number of methyl groups, the N—C bond length from the *ab initio* calculations decreases to 1.503 Å for dimethylammonium (3) and 1.499 Å for trimethylammonium (4). Shorter bond lengths for 3 and 4 are also predicted by MM3. This can be attributed to the “electronegativity effect” in which the carbon atom in the newly introduced methyl group is more electronegative than nitrogen, and the bond lengths of other N—C bonds (actually, they are indistinguishable) are shortened. With one more methyl group, however, tetramethylammonium (5) carries a longer N—C bond length than trimethylammonium (4), which is, more than likely, due to steric overcrowding. MM3 also well-reproduces N—H bond lengths, whereas the deviations of the C—H bonds are relatively large. Because the equilibrium bond length and the stretching force constant for the C—H bond are part of the MM3 skeleton parameters which have already been established, the only means that can be used to reproduce the C—H-associated properties, for example, C—H bond lengths and C—H stretching frequencies, is through electronegativity parameters that describe the chemical environmental changes caused by the neighboring atoms. The electronegativity parameter, however, affects both the C—H bond length

and the C—H stretching force constant simultaneously with a predefined ratio in MM3 that is an adjustable parameter. After considering the overall effect, the electronegativity parameter was selected such that the vibrational frequencies associated with the C—H stretching are well reproduced, whereas the C—H bond lengths carry small systematic deviations.

All molecular mechanics and *ab initio* bond angles involved in the ammonium ion methyl derivatives are in close agreement, with an average deviation of 0.2° and a maximum deviation of 0.4°. When the vibrational frequencies were compared between the two calculations, as shown in the tables, it is observed that methylammonium (2) and dimethylammonium (3) (with root-mean-square deviations of 45 and 40 cm<sup>-1</sup>) carry larger deviations than trimethyl and tetramethyl derivatives (root-mean-square deviations of 31 and 24 cm<sup>-1</sup>). Most of the deviations are from the vibrational modes associated with N—C—H bending. For those modes, MM3 has higher frequencies than Gaussian for methylammonium (2) and lower frequencies for dimethylammonium (3). Both methods agree with each other for trimethyl and tetramethyl derivatives (4 and 5, respectively).

### ETHYLAMMONIUM (6)

Bond lengths, bond angles, torsion angles, and vibrational frequencies for ethylammonium (6) are shown in Table VII. For similar reasons discussed above, C—H bond lengths were partially sacrificed to accommodate the vibrational frequencies involving the C—H stretching mode. The average C—H bond length deviations are 0.010 Å and 0.014 Å for methylene and methyl groups, respectively. While the MM3 bond lengths between heavy atoms are well within the acceptable range with deviations of 0.004 Å for N—C and 0.006 Å for C—C bonds, MM3 calculated an N—H bond length 0.008 Å shorter than the MP2/6-31 + G\* value. The average deviation of bond angles is 0.6° between the MM3 and *ab initio* calculations. As shown in Table VII, two different H—N—C angles exist, depending the torsion angles of H—N—C—C. When the torsion angle is 180° (*trans*), MM3 underestimates the H—N—C angle by 0.6°; and when the torsion angle is about 60° (*gauche*), MM3 overestimates the bond angle by 0.7°. This systematic error is presumably caused by the torsion-bending interaction that is not included in the MM3 potential function. Due to steric repulsion, the two bond angles increase when the tor-

TABLE III.  
Geometrical Data and Vibrational Frequencies of Methylammonium.

	Gaussian	MM3	Deviation
Bonds			
C(1)—N(+)(2)	1.510	1.515	0.005
C(1)—H (average)	1.088	1.101	0.013
N(+)—H (average)	1.028	1.024	−0.004
Angles			
N(+)(2)—C(1)—H (average)	108.2	108.1	−0.1
C(1)—N(+)(2)—H (average)	111.6	111.6	0.0
Modes			
Asym. N—H str.	3347	3347	−0.
Asym. N—H str.	3347	3347	−0.
Sym. N—H str.	3249	3249	0.
Asym. C—H str.	3116	3101	−15
Asym. C—H str.	3116	3101	−15
Sym. C—H str.	3001	2980	−20
H—N—H bend	1632	1619	−13
H—N—H bend	1632	1619	−13
NH3 + CH3 umbrella	1508	1482	−26
H—C—H bend	1466	1427	−39
H—C—H bend	1466	1427	−39
CH3 + NH3 umbrella	1435	1366	−69
N—C—H bend	1243	1143	−101
N—C—H bend	1243	1143	−101
N—C—H + C—N—N bend	925	956	31
C—N—H + N—C—H bend	886	956	70
N—C str.	886	921	35
H—N—C—H torsion	293	300	7
		rms	45

sion angle decreases from 180° to 0°. However, in MM3, the van der Waals interaction, coupled with the bending and torsional energy equations, is not adequate to address the bond angle change as a function of the torsion angle. The present study, along with previous investigations, indicates that introducing an explicit torsion–bending term is necessary to further improve the performance of MM3 calculations. MM3 and *ab initio* calculations are in reasonably good agreement on the vibrational frequencies for all the modes except the two involving wagging and rocking for both NH<sub>3</sub> and CH<sub>3</sub>. Those modes can be further broken down to N—C—H and C—N—H bending and controlled by these two bending force constants. The root-mean-square deviation for all 27 modes is 42 cm<sup>−1</sup>.

PROPYLAMMONIUM (7, 8)

Both *ab initio* and molecular mechanics calculated results for *trans* and *gauche* propylammo-

nium (7 and 8, respectively) are listed in Tables VIII and IX. The discrepancies between the MP2/6-31 + G\* and MM3 calculated bond lengths are relatively small with an average deviation of 0.005 Å for both conformers. Compared with the methyl and ethyl derivatives, propylammonium ions carry relatively larger bond angle deviations. The *trans* propylammonium ion (7) has an average deviation of 0.9° and a maximum deviation of 1.5°, whereas the *gauche* conformer (8) carries an average deviation of 0.8° and the maximum deviation of 1.2°. Two skeletal bond angles (formed by heavy atoms), N—C—C and C—C—C, exist in propylammonium. As discussed above, two bond angles are a function of the torsion angle N—C—C—C. As shown in the tables, from the Gaussian calculations, the C—C—C bond angle is 110.6° for the *trans* conformer (7) and 114.0° for the *gauche* conformer (8). This trend is the same as the one discussed above, which is due to the steric repulsion between the 1, 4 groups (here, NH<sub>3</sub> and CH<sub>3</sub>

**TABLE IV.**  
**Geometrical Data and Vibrational Frequencies of Dimethylammonium.**

	Gaussian	MM3	Deviation
<b>Bonds</b>			
N(+)(2)—H (average)	1.028	1.022	−0.006
N(+)(2)—C(4)	1.503	1.509	0.006
N(+)(2)—C(5)	1.503	1.509	0.006
C—H (average)	1.090	1.101	0.011
<b>Angles</b>			
H(1)—N(+)(2)—H(3)	105.6	105.6	0.0
H—N(+)(2)—C (average)	109.2	109.1	−0.1
C(4)—N(+)(2)—C(5)	113.9	114.3	0.4
N(+)—C—H (average)	108.2	108.1	−0.1
<b>Modes</b>			
Asym. N—H str.	3331	3317	−14
Sym. N—H str.	3269	3262	−7
Asym. C—H str.	3104	3105	2
Asym. C—H str.	3103	3105	2
Asym. C—H str.	3101	3102	1
Asym. C—H str.	3101	3100	−1
Sym. C—H str.	2990	2983	−7
Sym. C—H str.	2989	2982	−7
H—N—H bend	1625	1604	−21
NH <sub>2</sub> rock	1472	1468	−4
H—C—H bend	1471	1443	−28
H—C—H bend	1459	1434	−25
H—C—H bend	1458	1426	−32
H—C—H bend	1444	1423	−21
CH <sub>3</sub> umbrella	1419	1387	−32
CH <sub>3</sub> umbrella + NH <sub>2</sub> rock	1391	1341	−51
NH <sub>2</sub> twist	1347	1265	−83
CH <sub>3</sub> rock	1241	1169	−72
CH <sub>3</sub> wag	1213	1162	−51
CH <sub>3</sub> rock	1048	1131	83
CH <sub>3</sub> wag	996	1102	106
Asym. N—C str.	985	953	−33
Sym. N—C str.	843	837	−6
NH <sub>2</sub> wag	794	821	27
C—N—C bend	373	394	21
CH <sub>3</sub> torsion	263	261	−3
CH <sub>3</sub> torsion	190	208	18
		rms	40

groups). MM3 reproduces this bond angle change reasonably well without an explicit torsion-bending energy term. Compared to the bond angle change of 3.4° in our *ab initio* calculations, MM3 gave 2.6°. The bond angle N—C—C, on the other hand, has the same value for *trans* and *gauche* conformations, according to the *ab initio* calculations, whereas MM3 predicted the *gauche* conformer (8) to be 2.0° larger than the *trans* one (7). For both conformers, MM3 and Gaussian show

sufficiently good agreement on the vibrational frequencies with root-mean-square deviations of 41 and 36 cm<sup>−1</sup>, respectively.

### ETHYLMETHYLAMMONIUM (9, 10)

*Trans*-ethylmethylammonium (9), *gauche*-ethylmethylammonium (10), and *trans*-ethyldimethylammonium (11), were used for cases of ammonium ions with both ethyl and methyl substitu-

**TABLE V.**  
**Geometrical Data and Vibrational Frequencies of Trimethylammonium.**

	Gaussian	MM3	Deviation
Bonds			
N(+)(2)—C (average)	1.499	1.507	1.008
C—H (average)	1.090	1.099	0.009
N(+)(2)—H(5)	1.029	1.023	−0.006
Angles			
N(+)—C—H (average)	108.2	108.1	−0.1
C—N(+)—C (average)	111.5	111.7	0.2
C—N(+)—H (average)	107.3	107.1	−0.2
Modes			
N—H str.	3279	3259	−20
Asym. C—H str.	3094	3109	16
Asym. C—H str.	3094	3108	14
Asym. C—H str.	3091	3108	17
Asym. C—H str.	3091	3106	14
Asym. C—H str.	3091	3106	15
Asym. C—H str.	3091	3103	12
Sym. C—H str.	2983	2986	3
Sym. C—H str.	2981	2986	5
Sym. C—H str.	2981	2986	5
H—C—H bend	1483	1463	−20
H—C—H bend	1469	1460	−9
H—C—H bend	1469	1460	−9
H—C—H bend	1455	1431	−24
H—C—H bend	1455	1431	−24
H—C—H bend	1453	1423	−31
CH3 umbrella, C—N—N bend	1440	1417	−22
CH3 umbrella, C—N—H bend	1415	1417	2
CH3 umbrella	1415	1396	−19
CH3 umbrella, C—N—H bend	1386	1332	−54
CH3 umbrella, C—N—H bend	1386	1332	−54
CH3 rock, CH3 wag	1245	1192	−53
CH3 rock, CH3 wag	1218	1192	−27
CH3 rock, CH3 wag	1218	1188	−31
CH3 rock	1043	1105	62
CH3 rock	1024	1105	81
CH3 wag	1024	1101	77
Asym. N—C str.	958	932	−27
Sym. N—C str.	958	932	−27
Sym. N—C str.	781	762	−19
N(CH3)3 umbrella	447	439	−8
C—N—C bend	384	394	10
C—N—C bend	384	394	10
CH3 torsion	254	253	−1
CH3 torsion	254	253	−1
CH3 torsion	172	208	36
		rms	31

**TABLE VI.**  
**Geometrical Data and Vibrational Frequencies of Tetramethylammonium.**

	Gaussian	MM3	Deviation
<b>Bonds</b>			
N(+)—C (average)	1.503	1.508	0.005
C—H (average)	1.091	1.099	0.008
<b>Angles</b>			
N(+)—C—H (average)	108.8	108.4	−0.4
C—N(+)—C (average)	109.5	109.5	−0.0
<b>Modes</b>			
Asym. C—H str.	3087	3113	26
Asym. C—H str.	3087	3113	26
Asym. C—H str.	3087	3113	26
Asym. C—H str.	3084	3112	28
Asym. C—H str.	3084	3112	28
Asym. C—H str.	3082	3109	27
Asym. C—H str.	3082	3109	27
Asym. C—H str.	3082	3109	27
Sym. C—H str.	2979	2991	12
Sym. C—H str.	2974	2990	16
Sym. C—H str.	2974	2990	16
Sym. C—H str.	2974	2990	16
H—C—H bend	1482	1479	−3
H—C—H bend	1482	1479	−3
H—C—H bend	1482	1479	−3
H—C—H bend	1465	1433	−32
H—C—H bend	1452	1433	−19
H—C—H bend	1452	1433	−19
H—C—H bend	1439	1430	−9
H—C—H bend	1439	1430	−9
CH3 umbrella	1439	1409	−29
CH3 umbrella	1413	1401	−12
CH3 umbrella	1413	1401	−12
CH3 umbrella	1413	1401	−12
N—C str., H—C—N bend	1275	1254	−20
N—C str., H—C—N bend	1275	1254	−20
N—C str., H—C—N bend	1275	1254	−20
H—C—N bend	1148	1118	−31
H—C—N bend	1148	1118	−31
H—C—N bend	1046	1097	51
H—C—N bend	1046	1097	51
H—C—N bend	1046	1097	51
Asym. N—C str.	935	917	−18
Asym. N—C str.	935	917	−18
Asym. N—C str.	935	917	−18
Sym. N—C str.	721	693	−28
C—N—C bend	448	432	−16
C—N—C bend	448	432	−16
C—N—C bend	448	432	−16
C—N—C bend	354	357	3
C—N—C bend	354	357	3
CH3 torsion	287	279	−7
CH3 torsion	287	279	−7
CH3 torsion	287	279	−7
CH <sub>3</sub> torsion	165	210	45
		rms	24

**TABLE VII.**  
**Geometrical Data and Vibrational Frequencies of Ethylammonium.**

	Gaussian	MM3	Deviation
Bonds			
N(+)—H (average)	1.029	1.021	−0.008
N(+)(2)—C(4)	1.520	1.516	−0.004
C(4)—H (average)	1.091	1.101	0.010
C(4)—C(8)	1.515	1.521	0.006
C(8)—H (average)	1.094	1.108	0.014
Angles			
H—N(+)—H (average)	107.5	107.2	−0.3
H(1)—N(+)(2)—C(4)	112.3	111.7	−0.6
H(3)—N(+)(2)—C(4)	111.1	111.8	0.7
C—N(+)—H (average)	111.1	111.8	0.7
N(+)—C—H (average)	106.1	107.3	1.2
N(+)(2)—C(4)—C(8)	109.9	109.2	−0.7
H(6)—C(4)—H(7)	109.0	108.3	−0.7
C(4)—C(8)—H (average)	111.8	111.9	0.1
Torsions			
H(1)—N(+)(2)—C(4)—C(8)	180.0	−180.0	0.0
H(3)—N(+)(2)—C(4)—C(8)	59.6	59.8	0.2
H(5)—N(+)(2)—C(4)—C(8)	−59.6	−59.8	−0.2
Modes			
Asym. N—H str.	3345	3347	2
Asym. N—H str.	3344	3347	3
Sym. N—H str.	3241	3250	9
Asym. CH2 str.	3074	3064	−10
Asym. CH3 str.	3054	3020	−34
Asym. CH3 str.	3040	3019	−21
Sym. CH2 str.	3006	3002	−3
Sym. CH3 str.	2956	2925	−31
H—N—H bend	1628	1631	3
H—N—H bend	1623	1624	2
NH3 umbrella, CH2 rock	1494	1526	32
H—C—H bend	1480	1475	−5
H—C—H bend	1463	1462	−2
NH3 umbrella, CH2 rock	1462	1451	−11
H—C—H bend	1411	1436	25
NH3, umbrella, H—C—H bend	1371	1383	12
CH2 twist	1309	1317	8
NH3 wag, CH3 wag	1209	1064	−145
NH3 rock, CH3 rock	1166	1049	−117
N—C str., C—C str.	1004	1037	33
NH3 wag, CH3 wag	921	955	34
NH3 rock, CH3 rock	914	928	14
CH2 wag	821	849	27
N—C str., C—C str.	777	841	64
N—C—C bend	368	348	−20
CH3, NH3 torsion	268	277	8
CH3, NH3 torsion	212	224	12
		rms	42

**TABLE VIII.**  
**Geometrical Data and Vibrational Frequencies of *Trans*-Propylammonium.**

	Gaussian	MM3	Deviation
<b>Bonds</b>			
N(+)—H (average)	1.029	1.021	−0.008
N(+)(2)—C(4)	1.520	1.517	−0.003
C—N (average)	1.092	1.101	0.009
C(4)—C(8)	1.518	1.523	0.005
C(8)—C(10)	1.530	1.530	0.000
<b>Angles</b>			
H—N(+)—H (average)	107.5	107.2	−0.3
H—N(+)—C (average)	112.4	111.7	−0.7
N(+)—C—H (average)	106.3	107.2	0.9
N(+)(2)—C(4)—C(8)	110.4	109.5	−0.9
C(4)—C(8)—C(10)	110.6	111.9	1.5
<b>Torsions</b>			
H(1)N(+)(2)—C(4)—C(8)	180.0	180.0	0.0
N(+)(2)—C(4)—C(8)—C(10)	180.0	180.0	0.0
H(3)N(+)(2)—C(4)—C(8)	59.5	59.9	0.4
H(5)N(+)(2)—C(4)—C(8)	−59.5	−59.9	−0.4
H(6)—C(4)—C(8)—C(10)	−61.6	−61.1	0.5
H(7)—C(4)—C(8)—C(10)	61.6	61.1	−0.5
<b>Modes</b>			
Asym. N—H str.	3344	3347	3
Asym. N—H str.	3344	3347	3
Sym. N—H str.	3240	3250	11
Asym. CH <sub>2</sub> str.	3063	3064	2
Sym. CH <sub>2</sub> str.	3054	3002	−52
Asym. CH <sub>2</sub> str.	3041	2975	−66
Asym. CH <sub>3</sub> str.	2995	2969	−26
Asym. CH <sub>3</sub> str.	2988	2968	−20
Sym. CH <sub>2</sub> str.	2957	2922	−35
Sym. CH <sub>3</sub> str.	2939	2875	−64
H—N—H bend	1625	1631	6
H—N—H bend	1619	1626	6
NH <sub>3</sub> umbrella, CH <sub>2</sub> rock	1489	1542	53
NH <sub>3</sub> umbrella, CH <sub>2</sub> rock	1482	1474	−8
H—C—H bend	1471	1457	−14
H—C—H bend	1469	1456	−14
H—C—H bend	1464	1443	−20
H—C—H bend	1406	1439	33
H—C—H bend, CH <sub>3</sub> umbrella	1379	1402	23
CH <sub>3</sub> umbrella, CH <sub>2</sub> rock	1313	1358	46
CH <sub>2</sub> twist	1306	1330	24
CH <sub>2</sub> twist	1285	1243	−42
C—C str., NH <sub>3</sub> + CH <sub>3</sub> rock	1195	1074	−121
CH <sub>2</sub> + CH <sub>3</sub> + NH <sub>3</sub> wag	1157	1054	−103
C—C str., NH <sub>3</sub> + CH <sub>3</sub> rock	1034	1000	−34
CH <sub>3</sub> + NH <sub>3</sub> wag	975	982	7
C—C str., NH <sub>3</sub> rock	946	976	29
C—N str.	926	949	23
CH <sub>2</sub> wag	835	891	56
C—C str., NH <sub>3</sub> − CH <sub>3</sub> rock	833	846	13
CH <sub>2</sub> wag	742	798	57
C—C—C bend	414	375	−39
C—C—N bend	247	276	29
NH <sub>3</sub> + CH <sub>3</sub> torsion	240	253	13
NH <sub>3</sub> + CH <sub>3</sub> torsion	208	223	15
C—C—C—N torsion	114	135	20
		rms	41

**TABLE IX.**  
**Geometrical Data and Vibrational Frequencies of *Gauche*-Propylammonium.**

	Gaussian	MM3	Deviation
<b>Bonds</b>			
N(+)—H (average)	1.028	1.020	−0.008
N(+)(2)—C(4)	1.520	1.516	−0.004
C(4)—H (average)	1.093	1.101	0.008
C(4)—C(8)	1.519	1.524	0.005
C(8)—C(10)	1.529	1.531	0.002
<b>Angles</b>			
H—N(+)—H (average)	107.5	106.9	−0.7
H—N(+)—C (average)	112.1	111.6	−0.5
N(+)—C—H (average)	106.0	107.2	1.2
N(+)(2)—C(4)—C(8)	110.4	111.5	1.1
C(4)—C(8)—C(10)	114.0	114.5	0.5
<b>Torsions</b>			
H(1)—N(+)(2)—C(4)—C(8)	−178.7	−174.7	4.0
N(+)(2)—C(4)—C(8)—C(10)	−60.9	−64.0	−3.1
H(3)—N(+)(2)—C(4)—C(8)	61.0	65.3	4.3
H(5)—N(+)(2)—C(4)—C(8)	−58.3	−54.8	3.5
H(6)—C(4)—C(8)—C(10)	57.1	56.1	−1.0
H(7)—C(4)—C(8)—C(10)	−179.3	176.9	−2.4
<b>Modes</b>			
Asym. N—H str.	3349	3354	5
Asym. N—H str.	3346	3347	2
Sym. N—H str.	3244	3254	11
Asym. CH <sub>2</sub> str.	3062	3060	−2
Sym. CH <sub>2</sub> str.	3047	3000	−48
Asym. CH <sub>3</sub> str.	3019	2977	−43
Asym. CH <sub>2</sub> str.	3003	2971	−32
Asym. CH <sub>3</sub> str.	2993	2968	−25
Sym. CH <sub>2</sub> str.	2951	2921	−30
Sym. CH <sub>3</sub> str.	2938	2878	−60
H—N—H bend	1628	1638	10
H—N—H bend	1622	1626	4
NH <sub>3</sub> umbrella, CH <sub>2</sub> rock	1492	1544	53
NH <sub>3</sub> umbrella, CH <sub>2</sub> rock	1481	1482	1
H—C—H bend	1470	1477	7
H—C—H bend	1466	1467	1
NH <sub>3</sub> umbrella, H—C—H bend	1456	1453	−3
H—C—H bend	1408	1447	39
H—C—H bend	1378	1423	45
CH <sub>3</sub> umbrella, CH <sub>2</sub> rock	1350	1381	31
CH <sub>2</sub> twist	1303	1339	36
CH <sub>2</sub> twist	1271	1249	−23
C—C str.	1182	1077	−105
H—C—C bend	1126	1043	−82
H—C—C bend	1049	1019	−30
H—N—C bend	976	983	7
H—N—C bend	953	981	28
N—C str.	906	941	35
H—N—C bend, H—C—C bend	837	878	41
CH <sub>2</sub> wag	801	804	4
CH <sub>2</sub> wag	738	783	44
C—C—C bend	439	413	−25
H—C—C—H torsion	311	308	−3
NH <sub>3</sub> torsion, CH <sub>3</sub> torsion	254	281	27
NH <sub>3</sub> torsion, CH <sub>3</sub> torsion	204	212	8
N—C—C—C torsion	124	128	5
		rms	26



**TABLE X.**  
**Geometrical Data and Vibrational Frequencies of *Trans*-Ethylmethylammonium.**

	Gaussian	MM3	Deviation
<b>Bonds</b>			
C(1)—N(+)(2)	1.502	1.505	0.003
N(+)(2)—H (average)	1.029	1.020	−0.009
N(+)(2)—C(5)	1.513	1.510	−0.003
C(5)—C(9)	1.516	1.521	0.005
C(5)—H (average)	1.092	1.101	0.009
<b>Angles</b>			
N(+)(2)—C(1)—H (average)	108.9	108.4	−0.5
C(1)—N(+)(2)—H (average)	109.5	109.1	−0.4
C(1)—N(+)(2)—C(5)	114.6	114.4	−0.2
H(3)—N(+)(2)—H(4)	105.5	105.1	−0.4
H—N(+)—C (average)	108.7	109.4	0.7
N(+)(2)—C(5)—C(9)	110.6	109.9	−0.7
N(+)—C—H (average)	106.2	107.2	1.0
<b>Torsions</b>			
C(1)—N(+)(2)—C(5)—C(9)	180.0	180.0	0.0
H(3)—N(+)(2)—C(5)—C(9)	−57.2	−57.3	−0.1
H(4)—N(+)(2)—C(5)—C(9)	57.2	57.3	0.1
<b>Modes</b>			
Asym. N—H str.	3324	3318	−6
Sym. N—H str.	3259	3264	5
Asym. CH3 str.	3103	3105	2
Asym. CH3 str.	3098	3101	2
Asym. CH2 str.	3062	3068	6
Asym. CH3 str.	3051	3020	−31
Asym. CH3 str.	3036	3019	−17
Sym. CH2 str.	2994	3006	12
Sym. CH3 str.	2989	2982	−7
Sym. CH3 str.	2954	2925	−29
H—N—N bend	1622	1615	−7
CH <sub>2</sub> rock	1480	1538	58
H—C—H bend	1467	1478	10
H—C—H bend	1465	1462	−3
H—C—H bend	1463	1441	−22
H—C—H bend	1459	1436	−23
H—C—H bend	1431	1435	4
H—C—H bend	1409	1428	19
CH3 umbrella, NH2 rock	1397	1389	−7
CH3 umbrella, CH2 rock	1353	1354	1
CH2 twist	1338	1324	−13
NH2 twist	1285	1283	−2
CH3 rock	1212	1155	−57
H—C—N bend	1170	1133	−37
H—C—C bend	1045	1044	−2
CH3 rock	1014	1033	19
C—C str.	1005	987	−18
N—C str.	971	949	−23
CH2 wag	826	871	45
N—C str.	809	829	21
NH2 wag	762	805	43
C—N—C bend	417	387	−31
C—C—N bend	262	281	18
CH3 torsion	254	266	12
CH3 torsion	214	229	14
C—C—N—C torsion	99	115	16
		rms	23

**TABLE XI.**  
**Geometrical Data and Vibrational Frequencies of *Gauche*-Ethylmethyammonium.**

	Gaussian	MM3	Deviation
Bonds			
C(1)—N(+)(2)	1.503	1.507	0.004
N(+)—H (average)	1.029	1.020	−0.009
N(+)(2)—C(5)	1.517	1.512	−0.005
C(5)—C(9)	1.516	1.520	0.004
C—H (average)	1.093	1.101	0.008
Angles			
N(+)—C—H (average)	108.5	108.3	−0.2
C—N(+)—H (average)	108.7	108.5	−0.2
C(1)—N(+)(2)—C(5)	115.4	115.6	0.2
H(3)—N(+)(2)—H(4)	105.7	105.3	−0.4
H—N(+)—C (average)	108.6	108.7	0.1
N(+)(2)—C(5)—C(9)	111.8	110.9	−0.9
N(+)—C—H (average)	106.1	107.2	1.1
Torsions			
C(1)—N(+)(2)—C(5)—C(9)	63.6	69.8	6.2
H(3)—N(+)(2)—C(5)—C(9)	−174.0	−168.2	5.8
H(4)—N(+)(2)—C(5)—C(9)	−59.5	−53.7	5.8
Modes			
Asym. N—H str.	3325	3316	−9
Sym. N—H str.	3260	3261	2
Asym. CH3 str.	3114	3113	−2
Asym. CH3 str.	3096	3101	5
Asym. CH2 str.	3065	3063	−2
Asym. CH3 str.	3052	3028	−25
Asym. CH3 str.	3040	3019	−21
Sym. CH2 str.	2992	3001	8
Sym. CH3 str.	2990	2986	−4
Sym. CH3 str.	2958	2929	−29
H—N—H bend	1615	1618	3
CH <sub>2</sub> rock	1479	1525	46
H—C—H bend	1478	1486	9
H—C—H bend	1468	1465	−3
H—C—H bend	1462	1453	−9
H—C—H bend	1458	1446	−12
H—C—H bend	1429	1441	13
H—C—H bend	1417	1428	11
CH3 umbrella	1391	1395	5
CH3 umbrella, NH2 rock	1378	1365	−13
CH2 twist	1328	1339	11
NH2 twist	1287	1284	−3
CH3 rock	1201	1151	−50
H—C—C bend	1167	1133	−33
H—C—C bend	1065	1046	−20
H—C—C bend, H—C—N bend	1023	1038	15
C—C str.	1012	999	−13
N—C str., C—C str.	940	938	−2
CH2 wag	827	866	39
NH2 wag	779	804	25
N—C str., C—C str.	764	780	16
C—N—C bend	432	416	−15
C—N—C bend, CH3 torsion	315	326	11
CH3 torsion	280	275	−4
CH3 torsion	205	220	15
C—C—N—C torsion	103	107	3
		rms	19

**TABLE XII.**  
**Geometrical Data and Vibrational Frequencies of *Trans*-Ethylidimethylammonium.**

	Gaussian	MM3	Deviation
<b>Bonds</b>			
H(1)—N(+)(2)	1.029	1.021	−0.008
N(+)(2)—C(3)	1.520	1.512	−0.008
N(+)(2)—C(4)	1.501	1.505	0.004
N(+)(2)—C(5)	1.501	1.505	0.004
C—H (average)	1.093	1.102	0.009
C—C (average)	1.516	1.520	0.004
<b>Angles</b>			
H(1)—N(+)(2)—C(3)	105.5	105.7	0.2
H(1)—N(+)(2)—C(4)	106.6	105.9	−0.7
H(1)—N(+)(2)—C(5)	106.6	105.9	−0.7
C(3)—N(+)(2)—C(4)	113.1	113.4	0.3
C(3)—N(+)(2)—C(5)	113.1	113.4	0.3
C(4)—N(+)(2)—C(5)	111.3	111.8	0.5
N(+)(2)—C(3)—H(6)	105.7	107.0	1.3
N(+)(2)—C(3)—C(8)	113.9	113.1	−0.8
H(6)—C(3)—H(7)	108.3	107.2	−1.1
H(6)—C(3)—C(8)	111.4	111.1	−0.3
N(+)(2)—C(4)—H(15)	108.9	108.5	−0.4
<b>Torsions</b>			
H(1) L — N(+)(2)—C(3)—C(8)	−180.0	−180.0	0.0
C(4) L — N(+)(2)—C(3)—C(8)	−63.9	−64.4	−0.5
C(5)—N(+)(2)—C(3)—C(8)	63.9	64.4	0.5
<b>Modes</b>			
N—H str.	3267	3249	−18
Asym. CH <sub>3</sub> str.	3106	3117	11
Asym. CH <sub>3</sub> str.	3092	3116	24
Asym. CH <sub>3</sub> str.	3090	3105	15
Asym. CH <sub>3</sub> str.	3088	3103	16
Asym. CH <sub>2</sub> str.	3064	3059	−5
Asym. CH <sub>3</sub> str.	3046	3034	−12
Asym. CH <sub>3</sub> str.	3036	3022	−14
Sym. CH <sub>2</sub> str.	2985	3001	15
Sym. CH <sub>3</sub> str.	2983	2989	6
Sym. CH <sub>3</sub> str.	2980	2989	9
Sym. CH <sub>3</sub> str.	2956	2934	−22
CH <sub>2</sub> rock	1484	1544	60
H—C—H bend	1478	1497	19
H—C—H bend	1468	1475	7
H—C—H bend	1467	1465	−2
H—C—H bend	1463	1462	−0
H—C—H bend	1455	1451	−4
H—C—H bend	1445	1446	1
H—C—H bend	1438	1433	−5
CH <sub>3</sub> umbrella, H—N—C bend	1415	1430	14
H—C—H bend	1404	1419	15
CH <sub>3</sub> umbrella, H—C—H bend	1389	1407	18
CH <sub>2</sub> twist	1383	1374	−9
CH <sub>3</sub> umbrella, H—N—C bend	1349	1371	22
H—N—C bend, CH <sub>3</sub> umbrella	1292	1336	43
H—N—C bend, H—C—N bend	1217	1205	−12

(Continued)

TABLE XII.  
(Continued)

	Gaussian	MM3	Deviation
Modes			
H—C—N bend	1207	1159	−48
H—C—N bend	1168	1140	−28
H—C—N bend	1063	1103	40
H—C—N bend	1047	1047	−0
H—C—N bend	1021	1030	9
H—C—C bend, C—C str.	1004	1005	1
H—C—N bend	973	960	−14
N—C str.	902	891	−11
CH2 wag	797	835	38
N—C str.	749	720	−29
C—N—C bend	458	474	16
C—N—C bend	423	398	−25
C—N—C bend	387	388	1
CH3 torsion	293	292	−1
CH3 torsion	256	285	29
N—C—C bend, CH3 torsion	223	251	29
CH3 torsion	195	215	20
C—N—C—C torsion	83	94	11
		rms	21

tions. The geometry and vibrational frequencies from both the MP2/6-31 + G\* and MM3 calculations are shown in Tables X–XII. Overall, Gaussian and MM3 are in an excellent agreement for all three training molecules. The average bond length deviation for the three molecules is 0.006 Å. The largest discrepancy between the two methods is 0.009 Å. Comparing the N—C bond lengths between the two conformers of ethylmethyllumonium, they vary under different chemical environments. Gaussian results indicate that N—C<sub>methyl</sub> bond lengths are shorter than the N—C<sub>ethyl</sub> bond lengths, and MM3 follows this trend. Additionally, when the torsion angle C—N—C—C changes from 180° to 0°, the bond lengths of both N—C<sub>methyl</sub> and N—C<sub>ethyl</sub>, as well as C—C, should increase, which is mainly due to the 1,4 nonbonded interactions. Both Gaussian and MM3 reflect these changes satisfactorily, even if the explicit stretching–torsion cross-energy term is not used. The average bond angle deviations are 0.6° and 0.0° for *trans* and *gauche* ethylmethyllumonium, respectively, whereas the one for *trans*-ethyldimethyllumonium (11) is −0.1°. Two skeletal bond angles, C—N—C and N—C—C, exist for ethylmethyllumonium. Again, for the same reason, these angles should vary according to the changes of torsion angle C—N—C—C, with larger bond angles for the *trans* conformer and smaller bond angles for

the *gauche* conformer (10). Gaussian calculates the C—N—C bond angles of 114.6° and 115.4° for the *trans* and *gauche* ethylmethyllumonium, respectively, while the corresponding MM3 calculations give 114.4° and 115.6°. Similarly, for the N—C—C bond angle, *ab initio* and MM3 calculate the bond angle for the *trans* conformer (9) to be 1.2° and 1.0°, respectively, smaller than the *gauche* conformer (10). As an integrated part of the force field development, the deviation of vibrational frequencies between the *ab initio* and MM3 calculations was closely monitored. Using the final parameter set, MM3 is able to reproduce the scaled Gaussian frequencies with root-mean-square deviations of 23, 19, and 21 cm<sup>−1</sup>.

Conclusion

Eleven training molecules containing the ammonium moiety were calculated using Gaussian94 for both the optimum molecular geometries and vibrational frequencies on the MP2/6-31 + G\* level of theory. Based on the *ab initio* calculations, as well as torsional energy profiles calculated with the same level of theory, the MM3 force field was extended to ammonium and alkylammonium and protonated polyamines. The Parameter Analysis and Refinement Toolkit System (PARTS) was used

and proved to be an important utility program. The new parameters, which have been incorporated into MM3(96), will provide the basis for calculations, which, although beyond the capability of *ab initio* methods, will greatly enhance the understanding of conformational behaviors of polyamines by enabling quantitative structure–activity relationship investigations, already actively being pursued in our laboratories. Furthermore, these parameters provide the starting point for our modeling of zwitterionic analogs of glycine at the strychnine-insensitive glycine site.

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